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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,364	06/09/2006	**Filippo G. Giancotti**	MSK.P-082	5691

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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
02/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,364	GIANCOTTI, FILIPPO G.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 13-24* is/are pending in the application.

4a) Of the above claim(s) *4,5,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6, 7, 13-20, 23, and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed November 2, 2009 in response to the Office Action of May 1, 2009, is acknowledged and has been entered. Claims 1-7, 13-24 are pending. Claims 1, 16, 17, 24 are amended. Claims 8-12 are canceled. Claims 4, 5, 21, 22 remain withdrawn. Claims 1-3, 6, 7, 13-20, 23, and 24 are currently being examined as drawn to the elected species of breast cancer and antibody therapeutic agent.

New Rejections

(necessitated by amendments)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-3, 6, 7, 13-20, 23, and 24 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation drawn to targeting and inhibiting "**the signaling portion of the beta 4 portion of the integrin**" has no clear support in the specification and the claims as originally filed. THIS IS A NEW MATTER REJECTION.

Applicants do not point to support for the newly added claim limitation. A review of the specification fails to reveal support for a "signaling portion of beta 4" or any structures defined as such.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-3, 6, 7, 13-20, 23, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 16 recite the limitation **"the signaling portion"**. There is insufficient antecedent basis for this limitation in the claim.

Maintained Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. **Claims 1-3, 6, 7, 13-20, 23, and 24 remain rejected under 35 U.S.C. 102(b)** as being anticipated by US Patent Application Publication 2003/0224993 A1, Land et al, filed March 17, 2003, published December 4, 2003 (IDS); as evidenced by Mercurio et al (Seminars in Cancer Biology, 2001, 11:129-141) and Lee et al (Clinical Cancer Research, 2005, 11:2222-2228) (see section 5 of the previous Office Action).

Land et al teach a method of treating cancer in a patient comprising administering to the patient an antibody targeted to beta 4 to inhibit beta 4 integrin function or reduce the amount of active beta 4, wherein the administration is local to the

cancer cells, wherein the patient is human, wherein the cancer is breast cancer ([0047-0089]; [0311-0334]; [0340]; claims 1, 2, 5, 10, 13, 15, 18, 34, 41, 45, 62, 65, 66, 91, 92, and 96-101), said method further comprising administering a receptor protein tyrosine kinase inhibitor, wherein the inhibitor inhibits EGFR or ErbB2 or is Herceptin®, wherein EGFR and ErbB2 are active in oncogenesis ([0313-0314]; [0334]; [0340]; claims 34, 41, 62, 91, and 97). Land et al teach that the antibody targeted to beta 4 can inhibit ligand binding or reduce integrin-integrin receptor clustering or interaction, all of which are known to activate beta 4 signaling and induce cell proliferation, hence the antibody taught by Land et al would necessarily target and inhibit the signaling portion of beta 4 (claims 13, 15, 34, 91, and 92; [0039], [0048-49]; [0315-0328]; [0384]).

As evidenced by Mercurio et al, breast cancer expresses a6b4 (α6β4) (Table 1) and erbB2, wherein a6b4 associates with erbB2 in breast cancer (p. 135, col. 2). As evidenced by Lee et al breast cancer expresses MET (p. 2225, col. 2; Figure 2, Figure 3B, and Figure 4).

Response to Arguments

5. Applicants argue that Land teaches methods of inhibiting proliferation of certain cancer cells by contacting the b4 integrin with a composition that inhibits ligand binding. Applicants argue that inhibition of binding is not the same as inhibition of the signaling function, and there is no showing in the Land reference that any of the inhibitors there inhibit signaling. Applicants argue that Land is silent in its disclosure concerning

tumorigenesis, and actually demonstrates only an ability to retard growth in soft agar. Applicants argue that while growth is necessary for tumors to proceed, it is not sufficient as a predictor of tumorigenesis, which also requires an understanding of other properties including invasiveness. Since an anticipation rejection requires that each and every element, and since inherency can only be relied on where the undisclosed aspect must be present even if it is not mentioned, Applicants argue that the rejection for anticipation is not supported by the reference and should be withdrawn (p. 5).

The arguments have been considered but are not found persuasive. Antibodies that bind b4 and inhibit ligand binding or inhibit integrin-integrin receptor clustering or interaction clearly inhibit b4 signaling, as taught by Land above. Land teach the ligand binding or integrin-integrin receptor clustering or interaction initiates b4 signaling, and teach an antibody inhibiting ligand binding, integrin-integrin receptor clustering or interaction inhibits b4 signaling.

Applicants' assertion that Land is silent in its disclosure concerning tumorigenesis is incorrect. Land teach a method of treating cancer in a patient comprising administering to the patient an antibody targeted to beta 4 to inhibit beta 4 integrin function or reduce the amount of active beta 4 by targeting and inhibiting the signaling portion of b4, wherein the administration is local to the cancer cells, wherein the patient is human, wherein the cancer is breast cancer, as set forth above. Arguments drawn to the working example for inhibiting cell growth in soft agar in Land appear to be drawn to a question of enablement, however arguments drawn to enablement are irrelevant because Land teaches and anticipates all the claimed

limitations. Applicants also opine that tumor growth is not a predictor of tumorigenesis but provide no scientific basis for this opinion and are arguing limitations not recited in the claims. Land teaches all the claimed limitations for the reasons set forth above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. **Claims 1-3, 6, and 16-20 remain provisionally rejected** on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 7-9, 15, 17, 19, 21-22 of copending **Application No. 10/595845**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application and the instant application are claiming common

subject matter. The claims of both the copending application and the instant application are drawn to administering an antibody targeting beta 4 (β4) to a human who has a disease associated with angiogenesis, including breast cancer, wherein the breast cancer expresses α6β4.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

7. Applicants argue that the claims of application 10/595845 are directed to inhibition of angiogenesis, not inhibition of initiation of primary or metastatic tumor growth as in the present application. Applicants argue that the Examiner has not addressed the differences in the claims in making this rejection (p. 6).

The arguments have been considered but are not found persuasive. As stated previously, the claims of both the copending and instant application are drawn to administering the same agent (b4 integrin antibody to inhibit signaling of b4) to the same population of human patients that have a breast cancer to reduce the amount of active α6β4. Given the same agent is administered to the same population in the claimed methods of both applications, the methods would both necessarily inhibit initiation of primary or metastatic tumor growth and inhibit pathological angiogenesis as intended.

8. All other objections and rejections recited in the Office Action mailed May 1, 2009 are hereby withdrawn in view of amendments.

9. **Conclusion:** No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642